

09220617-122498

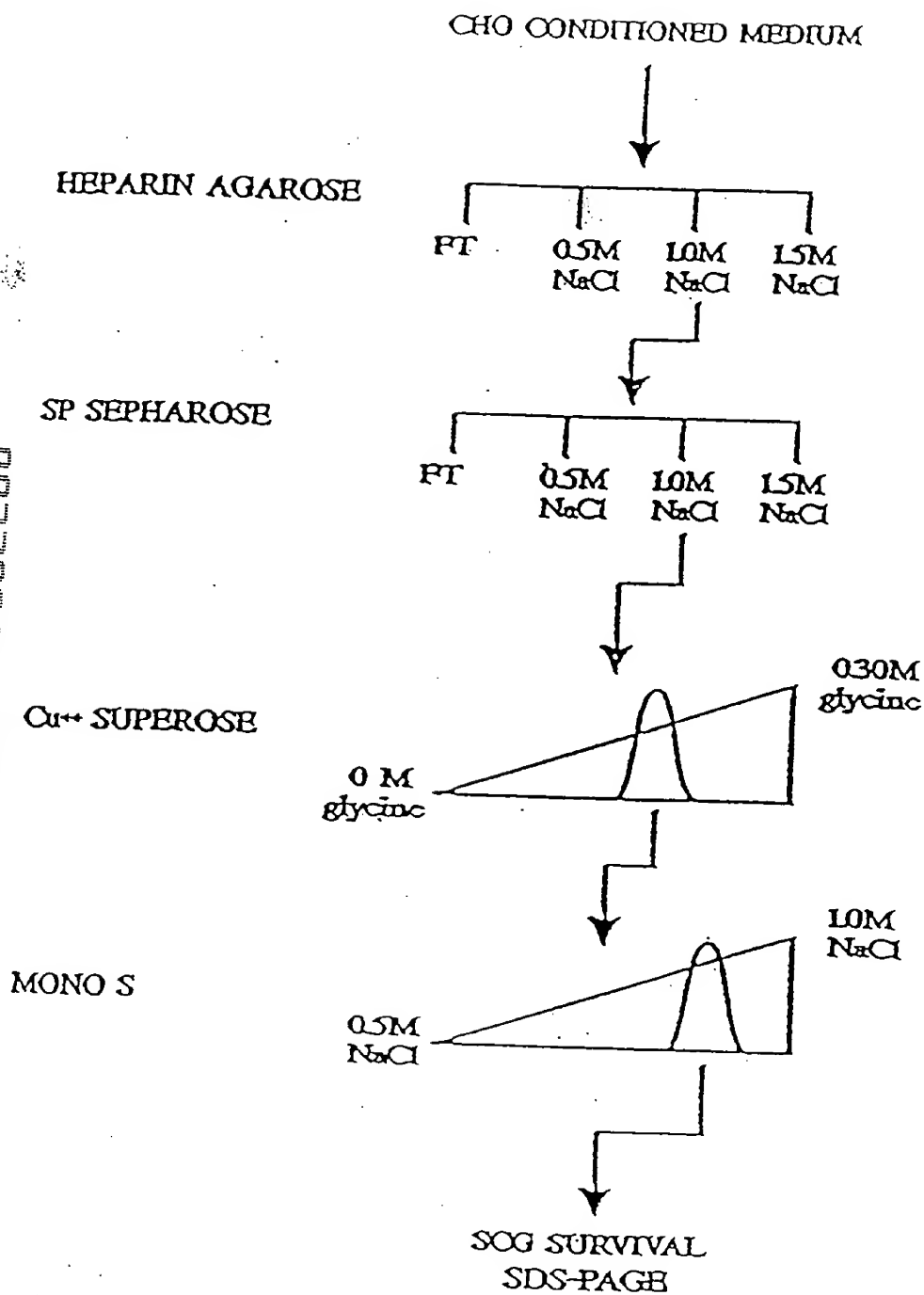


Figure 1

86422T" 4T902260

fraction: M L 21 22 23 24 25 26 27 28 29 30 31 32

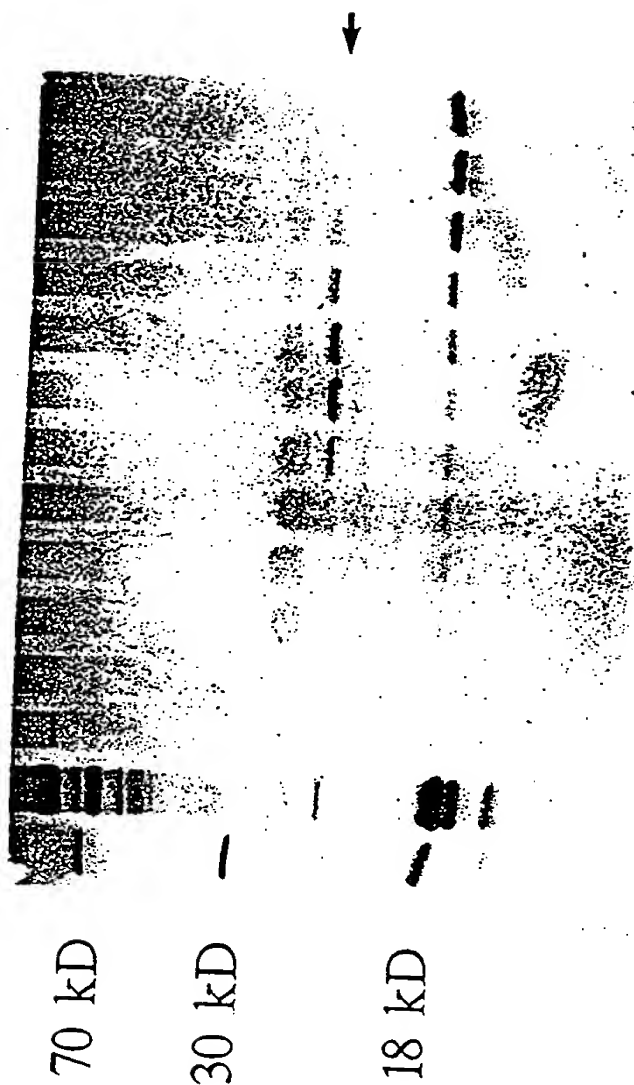


Figure 2a

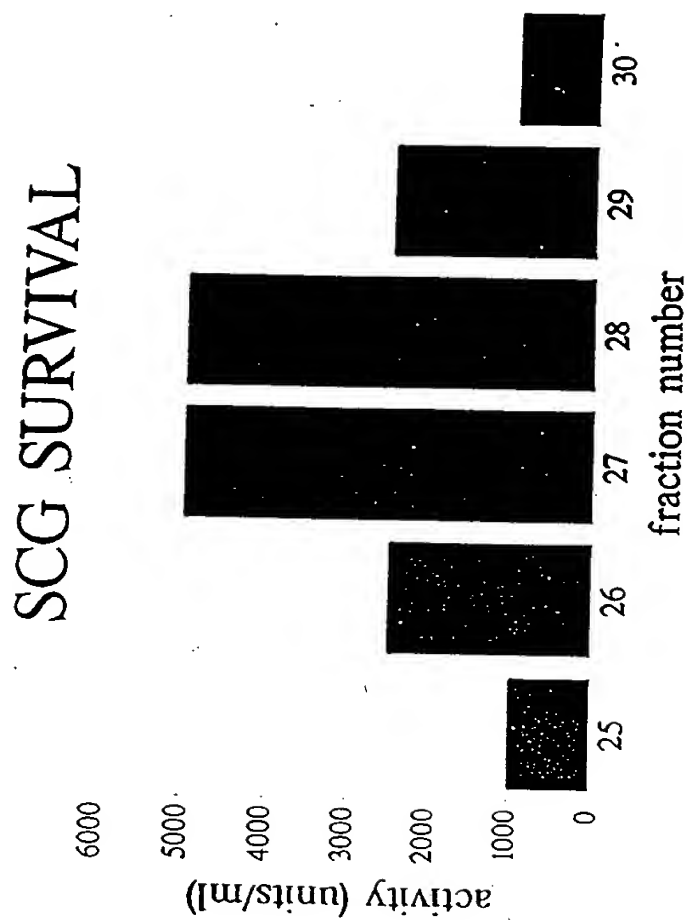


Figure 2b

09220617 122498 864221 71902260

Figure 3a NGF

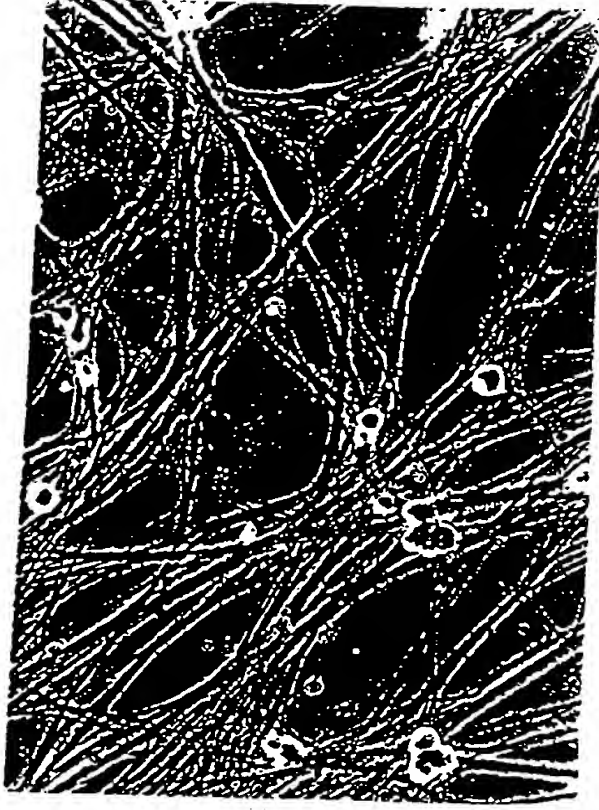


Figure 3b Anti-NGF

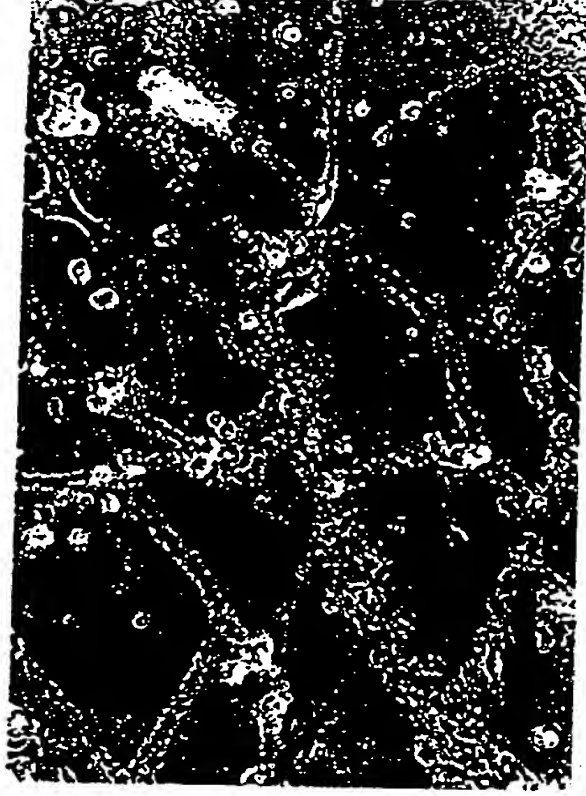
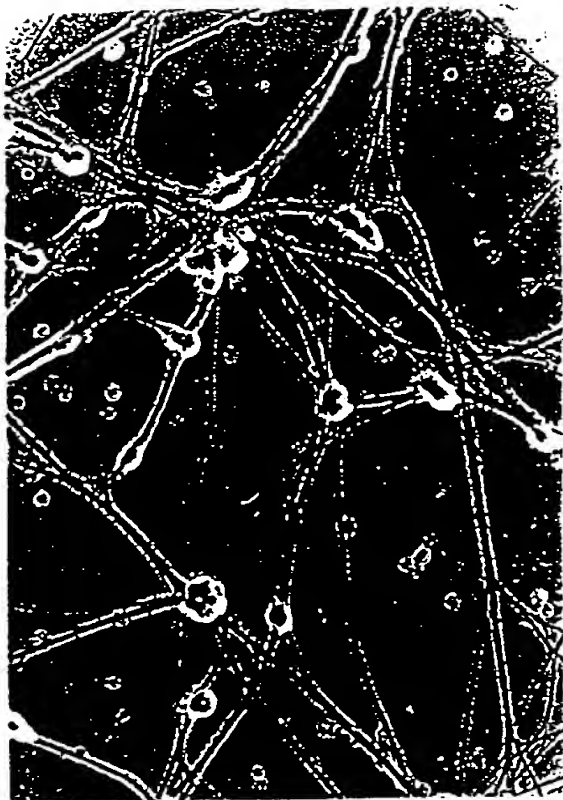


Figure 3c Anti-NGF
+
Neurturin



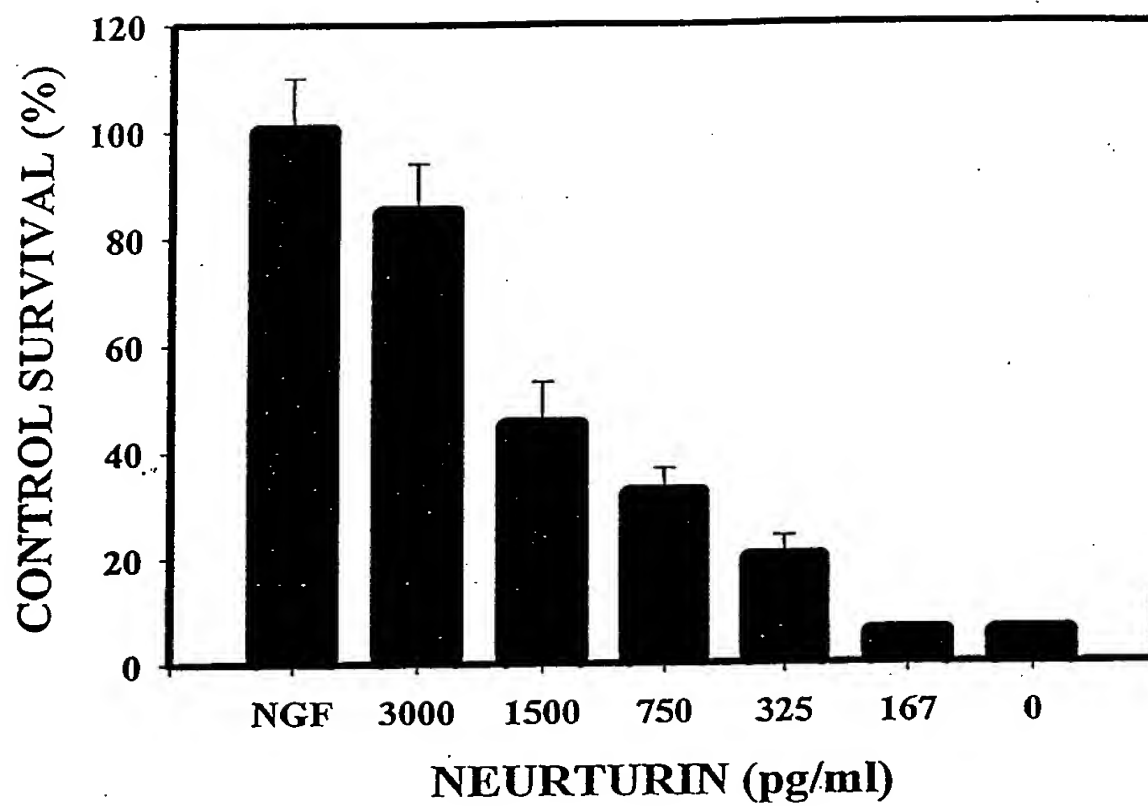


Figure 4

1	S	P	D	K	Q	M	A	V	L	P	R	R	E	R	N	R	Q	A	A	A	A	N	P	E	N	S	R	G	K	G	hGDNF	
1	S	P	D	K	Q	A	A	A	L	P	R	R	E	R	N	R	Q	A	A	A	A	S	P	E	N	S	R	G	K	G	mGDNF	
1	S	P	D	K	Q	A	A	A	L	P	R	R	E	R	N	R	Q	A	A	A	A	S	P	E	N	S	R	G	K	G	rGDNF	
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	hNTN	
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	mNTN	
31	R	R	G	Q	R	G	K	N	R	G	C	V	L	T	A	I	H	L	N	V	T	D	L	G	L	G	Y	E	T	K	hGDNF	
31	R	R	G	Q	R	G	K	N	R	G	C	V	L	T	A	I	H	L	N	V	T	D	L	G	L	G	Y	E	T	K	mGDNF	
31	R	R	G	Q	R	G	K	N	R	G	C	V	L	T	A	I	H	L	N	V	T	D	L	G	L	G	Y	E	T	K	rGDNF	
1	-	-	-	-	A	R	L	G	A	R	P	C	G	L	R	E	L	E	V	R	V	S	E	L	G	L	G	Y	A	S	D	hNTN
1	-	-	-	-	-	P	G	A	R	P	C	G	L	R	E	L	E	V	R	V	S	E	L	G	L	G	Y	T	S	D	mNTN	
61	E	E	L	I	F	R	Y	C	S	G	S	C	E	S	A	A	E	T	T	Y	D	K	I	L	K	N	L	S	R	N	R	hGDNF
61	E	E	L	I	F	R	Y	C	S	G	S	C	E	S	A	A	E	T	T	Y	D	K	I	L	K	N	L	S	R	S	R	mGDNF
61	E	E	L	I	F	R	Y	C	S	G	S	C	E	S	A	A	E	T	T	Y	D	K	I	L	K	N	L	S	R	S	R	rGDNF
28	E	T	V	L	F	R	Y	C	A	G	A	C	E	A	A	A	R	V	Y	D	L	G	L	R	R	L	R	Q	R	R	hNTN	
26	E	T	V	L	F	R	Y	C	A	G	A	C	E	A	A	A	I	R	I	Y	D	L	G	L	R	R	L	R	Q	R	R	mNTN
91	R	L	V	S	D	K	V	-	G	Q	A	C	C	R	P	I	A	F	D	D	D	L	S	F	L	D	D	N	L	V	hGDNF	
91	R	L	T	S	D	K	V	-	G	Q	A	C	C	R	P	V	A	F	D	D	D	L	S	F	L	D	D	N	L	V	mGDNF	
91	R	L	T	S	D	K	V	-	G	Q	A	C	C	R	P	V	A	F	D	D	D	L	S	F	L	D	D	S	L	V	rGDNF	
58	R	L	R	R	E	R	V	R	A	Q	P	C	C	R	P	T	A	Y	E	D	E	V	S	F	L	D	A	H	S	R	hNTN	
56	R	V	R	R	E	R	A	R	A	H	P	C	C	R	P	T	A	Y	E	D	E	V	S	F	L	D	V	H	S	R	mNTN	
120	Y	H	I	L	R	K	H	S	A	K	R	C	G	C	I	.	hGDNF															
120	Y	H	I	L	R	K	H	S	A	K	R	C	G	C	I	.	mGDNF															
120	Y	H	I	L	R	K	H	S	A	K	R	C	G	C	I	.	rGDNF															
88	Y	H	T	V	H	E	L	S	A	R	E	C	A	C	V	.	hNTN															
86	Y	H	T	L	Q	E	L	S	A	R	E	C	A	C	V	.	mNTN															

Figure 5

RT-PCR Analysis of Neurturin and GDNF

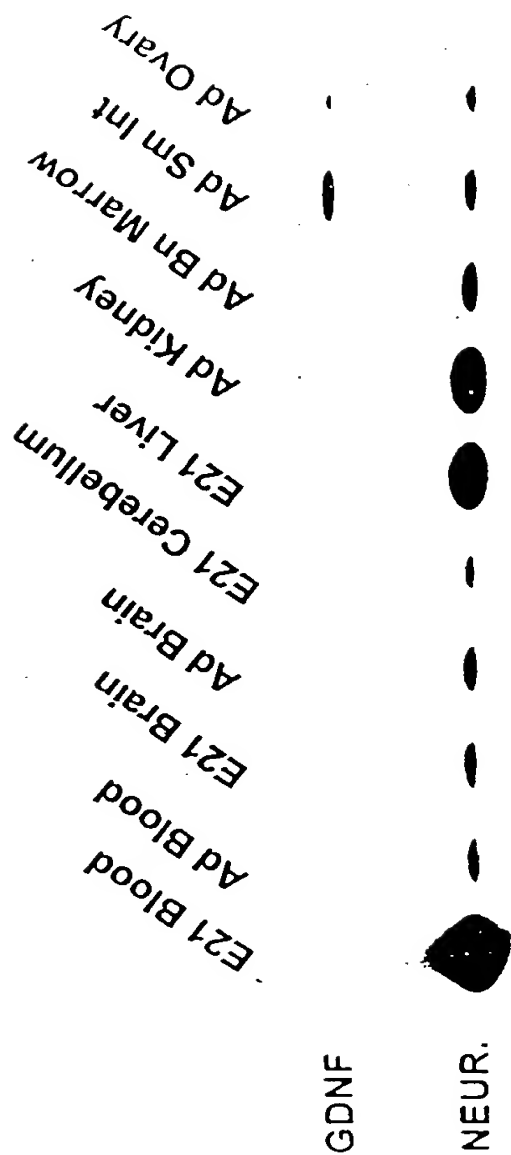


Figure 6

ATGCAGCGCTGGAAGGCGGGCGGCCTTGGCCTCAGTGCTCTGCAGCTCCGTGCTGTCCATC 60
Met Gln Arg Trp Lys Ala Ala Ala Leu Ala Ser Val Leu Cys Ser Ser Val Leu Ser Ile
 TGGATGTGTGCGAGAGGGCCTGCTTCTCAGCCACCGCCTCGGACCTGCGCTGGTCCCCTG 120
Trp Met Cys Arg Glu Gly Leu Leu Leu Ser His Arg Leu Gly Pro Ala Leu Val Pro Leu
 CACCGCCTGCCTCGAACCCTGGACGCCCCGATTGCCCGCCTGGCCCAGTACCGTGCACTC 180
His Arg Leu Pro Arg Thr Leu Asp Ala Arg Ile Ala Arg Leu Ala Gln Tyr Arg Ala Leu
 CTGCAGGGGGCCCCGGATGCGATGGAGCTGCGCGAGCTGACGCCCTGGGCTGGGCGGGCCC 240
Leu Gln Gly Ala Pro Asp Ala Met Glu Leu Arg Glu Leu Thr Pro Trp Ala Gly Arg Pro
 CCAGGTCCGCGCCGTGCGGGCGGGGCCCCGGCGGGCGCGCGCGCTGCGCGGTTGGGGGCG 300
Pro Gly Pro Arg Arg Arg Ala Gly Pro Arg Arg Arg Arg Ala Arg Ala Arg Leu Gly Ala
 CGGCCTTGCGGGCTGCGCGAGCTGGAGGTGCGCGTGAGCGAGCTGGGCCTGGGCTACGCG 360
Arg Pro Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Ala
 TCCGACGAGACGGTGCTGTCCGCTACTGCGCAGGCGCCTGCGAGGCTGCCGCGCGCGTC 420
Ser Asp Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ala Arg Val
 TACGACCTCGGGCTGCGACGACTGCGCCAGCGGCGGCGCCTGCGGCGGGAGCGGGTGCGC 480
Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Leu Arg Arg Glu Arg Val Arg
 GCGCAGCCCTGCTGCCGCCCGACGGCCTACGAGGACGAGGTGTCCTTCCTGGACGCGCAC 540
Ala Gln Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Ala His
 AGCCGCTACCACACGGTGACGAGCTGTGCGCGCGCGAGTGCGCCTGCGTGTGA 594
Ser Arg Tyr His Thr Val His Glu Leu Ser Ala Arg Glu Cys Ala Cys Val

Figure 7

ATGAGGCGCTGGAAGGCAGCGGCCCTGGTGTGCTCATCTGCAGCTCCCTGCTATCTGTC 60
Met Arg Arg Trp Lys Ala Ala Ala Leu Val Ser Leu Ile Cys Ser Ser Leu Leu Ser Val
 TGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGGGACCCGCGCTTGCCCCGCTA 120
Trp Met Cys Gln Glu Gly Leu Leu Leu Gly His Arg Leu Gly Pro Ala Leu Ala Pro Leu
 CGACGCCCTCCACGCACCCTGGACGCCCCGCATCGCCCGCCTGGCCCAGTATCGCGCTCTG 180
Arg Arg Pro Pro Arg Thr Leu Asp Ala Arg Ile Ala Arg Leu Ala Gln Tyr Arg Ala Leu
 CTCCAGGGCGCCCCGACGCGGTGGAGCTTCGAGAACTTTCTCCCTGGGCTGCCCCGATC 240
Leu Gln Gly Ala Pro Asp Ala Val Glu Leu Arg Glu Leu Ser Pro Trp Ala Ala Arg Ile
 CCGGGACCGCGCCGCTCGAGCGGGTCCCCGGCGTCGGCGGGCGCGGCCGGGGGGCTCGGCCT 300
Pro Gly Pro Arg Arg Arg Ala Gly Pro Arg Arg Arg Arg Ala Arg Pro Gly Ala Arg Pro
 TGTGGGCTGCGCGAGCTCGAGGTGCGCGTGAAGCGAGCTGGGCCTGGGCTACACGTCGGAT 360
Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Thr Ser Asp
 GAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGGCGGCCATCCGCATCTACGAC 420
Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ile Arg Ile Tyr Asp
 CTGGGCCTTCGGCGCCTGCGCCAGCGGAGGCGCGTGCGCAGAGAGCGGGCGCGGGCGCAC 480
Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Val Arg Arg Glu Arg Ala Arg Ala His
 CCGTGTGTGCGCCCGACGGCCTATGAGGACGAGGTGTCCTTCCTGGACGTGCACAGCCGC 540
Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Val His Ser Arg
 TACCACACGCTGCAAGAGCTGTCGGCGCGGGAGTGCGCGTGCCTGTGA 588
Tyr His Thr Leu Gln Glu Leu Ser Ala Arg Glu Cys Ala Cys Val

Figure 8

GGAGGGAGAGCGCGCGGTGGTTTCGTCCGTGTGCCCCGCGCCCGGCGC	-301
TCCTCGCGTGGCCCCGCGTCCTGAGCGCGCTCCAGCCTCCCACGCGCGCC	-251
ACCCCGGGGTTCACCTGAGCCCGGCGAGCCCGGGGAAGACAGAGAAAGAGA	-201
GGCCAGGGGGGAACCCCATGGCCCCGGCCCGTGTCCCGCACCCCTGTGCGG	-151
TGGCCTCCTCCGGCACGGGGTCCCCGGGTGCGCTCCGGTCCCCGCGATCC	-101
GGATGGCGCACGCAGTGGCTGGGGCCGGGCCGGGCTCGGGTGGTGGAGG	-51
AGTCACCACTGACCGGGTCATCTGGAGCCCGTGGCAGGCCGAGGCCAGG	-1
ATGAGGCGCTGGAAGGCAGCGGCCCTGGTGTGCTCATCTGCAGCTCCCT	50
GCTATCTGTCTGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGG	100
GACCCGCGCTTGCCCCGCTACGACGCCCTCCACGCACCCTGGAAGCCCGC	150
ATGCCCCGCTGGCCAGTATCGCGCTCTGCTCCAGGGCGCCCCCGACGC	200
GGTGGAGCTTCGAGAACTTTCTCCCTGGGCTGCCCCGCATCCCGGGACCGC	250
GCGCTGAGCGGGTCCCCGGCGTCGGCGGGCGCGGCCGGGGGCTCGGCCT	300
TGTGGGCTGCGCGAGCTCGAGGTGCGCGTGAGCGAGCTGGGCTGGGCTA	350
CACGTCGGATGAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGG	400
CGGCCATCCGCATCTACGACCTGGGCCTTOGGCGCCTGCGCCAGCGGAGG	450
CGCGTGCGCAGAGAGCGGGCGCGGGCGCACCCGTGTTGTGCCCCGACGGC	500
CTATGAGGACGAGGTGTCTTCTTGGACGTGCACAGCCGCTACACACGC	550
TGCAAGAGCTGTGCGCGCGGGAGTGCGCGTGCGTGATGCTACCTCACG	600
CCCCCGACCTGCGAAAGGGCCCTCCCTGCCGACCCTCGCTGAGAACTGA	650
CTTCACATAAAGTGTGGGAACTCCC	675

Figure 9

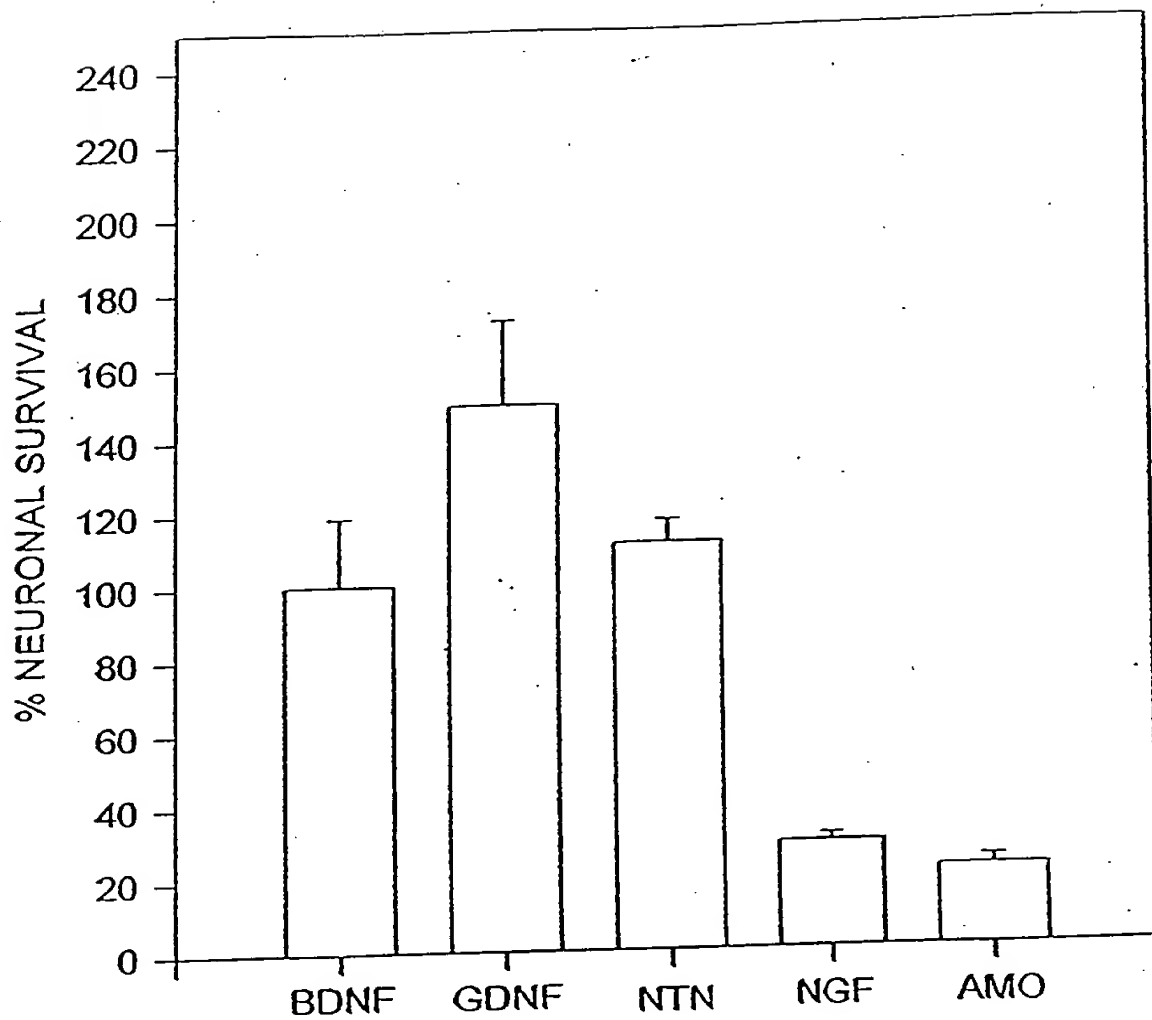


Figure 10

09220617.122498

GAGGGACCTGGACGCCCCATCAGGGTAAGAATTCTGGGGGCTCCCGACTCCCCAATTC	60
Glu Gly Pro Gly Arg Pro Ile Arg Val Arg Ile Pro Gly Gly Leu Pro Thr Pro Gln Phe	20
CTTCTCTCAAAGCCCTCACTTTGCCTTACAATCCTACTCTACCTTGCACTAGGTAACAAC	120
Leu Leu Ser Lys Pro Ser Leu Cys Leu Thr Ile Leu Leu Tyr Leu Ala Leu Gly Asn Asn	40
CATGTCCGTCTTCCAAGAGCCTTGGCTGGTTCATGCCGACTGTGGAGCCTGACCCTACCA	180
His Val Arg Leu Pro Arg Ala Leu Ala Gly Ser Cys Arg Leu Trp Ser Leu Thr Leu Pro	60
GTGGCTGAGCTGGGCCTGGGCTATGCCTCGGAGGAGAAGGTCATCTTCCGATACTGTGCT	240
Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu Glu Lys Val Ile Phe Arg Tyr Cys Ala	80
GGCAGCTGTCCCCAAGAGGCCCCGTACCCAGCACAGTCTGGTACTGGCCCCGGCTTCGAGGG	300
Gly Ser Cys Pro Gln Glu Ala Arg Thr Gln His Ser Leu Val Leu Ala Arg Leu Arg Gly	100
CGGGGTCGAGCCCATGGCCGACCCTGCTGCCAGCCCACCAGCTATGCTGATGTGACCTTC	360
Arg Gly Arg Ala His Gly Arg Pro Cys Cys Gln Pro Thr Ser Tyr Ala Asp Val Thr Phe	120
CTTGATGATCAGCACCATTTGGCAGCAGCTGCCTCAGCTCTCAGCTGCAAGCTTGTGGCTGT	420
Leu Asp Asp Gln His His Trp Gln Gln Leu Pro Gln Leu Ser Ala Ala Ala Cys Gly Cys	140
GGTGGCTGAAGGAGGCCAGTCTGGTGTCTCAGAATCACAAGCATGAGACAGGCTGGGCTT	480
Gly Gly	142
TGAAAGGCTCAGGTGACATTACTAGAAATTTGCATAGGTAAAGATAAGAAGGGAAAGGAC	540
CAGG	544

Figure 11

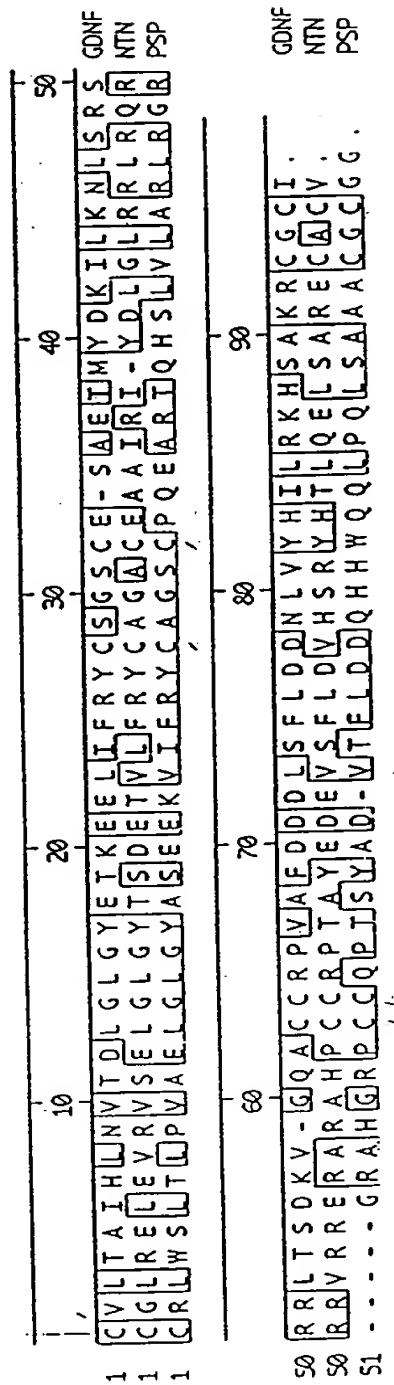


Figure 12

CCTCAGAGGAGAAGATTATCTTCCGATACTGTGCTGGCAGCTGTCCCCAAGAGGTCCGTACC 62
 Ser Glu Glu Lys Ile Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Gln Glu Val Arg Thr 20

CAGCACAGTCTGGTGCTGGCCCCGTCTTCGAGGGGCAGGGTCGAGCTCATGGCAGACCTTGC 122
 Gln His Ser Leu Val Leu Ala Arg Leu Arg Gly Gln Gly Arg Ala His Gly Arg Pro Cys 40

TGCCAGCCCACCAGCTATGCTGATGTGACCTTCCTTGATGACCACCACCATTTGGCAGCAG 182
 Cys Gln Pro Thr Ser Tyr Ala Asp Val Thr Phe Leu Asp Asp His His His Trp Gln Gln 60

CTGCCTCAGCTCTCAGCCGCAGCTTGTGGCTGTGGTGGCTGAAGGCGGCCAGCCTGGTCT 242
 Leu Pro Gln Leu Ser Ala Ala Ala Cys Gly Cys Gly Gly 73

CTCAGAATCACAAGCAAGAGGCAGCCTTTGAAAGGCTCAGGTGACGTTATTAGAAACTTG 302

CATAGGAGAAGATTAAGAAGAGAAAGGGGACCTG 336

09220617.122498

Figure 13

09220617-12498
86422T-1902260

<p>TGCCGGCTGTGGAGCCTGACCCTACCACTGGCTGAGCTTGGCCTGGGCTATGCCTCAGAG</p> <p>Cys Arg Leu Trp Ser Leu Thr Leu Pro Val Ala Glu Leu Gly Leu Gly Tyr Ala Ser Glu</p>	<p>60</p> <p>20</p>
<p>GAGAAGATTATCTTCCGATACTGTGCTGGCAGCTGTCCCCAAGAGGTCCGTACCCAGCAC</p> <p>Glu Lys Ile Ile Phe Arg Tyr Cys Ala Gly Ser Cys Pro Gln Glu Val Arg Thr Gln His</p>	<p>120</p> <p>40</p>
<p>AGTCTGGTGCTGGCCCGTCTTCGAGGGCAGGGTCGAGCTCATGGCAGACCTTGCTGCCAG</p> <p>Ser Leu Val Leu Ala Arg Leu Arg Gly Gln Gly Arg Ala His Gly Arg Pro Cys Cys Gln</p>	<p>180</p> <p>60</p>
<p>CCCACCAGCTATGCTGATGTGACCTTCCTTGATGACCACCACCATTTGGCAGCAGCTGCCT</p> <p>Pro Thr Ser Tyr Ala Asp Val Thr Phe Leu Asp Asp His His His Trp Gln Gln Leu Pro</p>	<p>240</p> <p>80</p>
<p>CAGCTCTCAGCCGCAGCTTGTGGCTGTGGTGGCTGAAGGCGGCCAGCCTGGTCTCTCAGA</p> <p>Gln Leu Ser Ala Ala Ala Cys Gly Cys Gly Gly</p>	<p>300</p> <p>91</p>
<p>ATCACAAGCAAGAGGCAGCCTTTGAAAGGCTCAGGTGACGTTATTAGAAACTTGCATAGG</p>	<p>360</p>
<p>AGAAGATTAAAGAAGAGAAAGGGGACCTGATT</p>	<p>391</p>

Figure 14

	10										20										30										40										
1	C	V	L	T	A	I	H	L	N	V	T	D	L	G	L	G	Y	E	T	K	E	E	L	I	F	R	Y	C	S	G	S	C	D	A	A	E	T	T	-	Y	GDNF(human)
1	C	V	L	T	A	I	H	L	N	V	T	D	L	G	L	G	Y	E	T	K	E	E	L	I	F	R	Y	C	S	G	S	C	E	A	A	E	T	M	-	Y	GDNF(rat)
1	C	V	L	T	A	I	H	L	N	V	T	D	L	G	L	G	Y	E	T	K	E	E	L	I	F	R	Y	C	S	G	S	C	E	S	A	E	T	M	-	Y	GDNF(mouse)
1	C	G	L	R	E	L	E	V	R	V	S	E	L	G	L	G	Y	A	S	D	E	T	V	L	F	R	Y	C	A	G	A	C	E	A	A	A	R	V	-	Y	NTN(human)
1	C	G	L	R	E	L	E	V	R	V	S	E	L	G	L	G	Y	T	S	D	E	T	V	L	F	R	Y	C	A	G	A	C	E	A	A	I	R	I	-	Y	NTN(mouse)
1	C	R	L	W	S	L	T	L	P	V	A	E	L	G	L	G	Y	A	S	E	E	K	I	I	F	R	Y	C	A	G	S	C	P	Q	E	V	R	T	Q	H	PSP(rat)
1	C	R	L	W	S	L	T	L	P	V	A	E	L	G	L	G	Y	A	S	E	E	K	V	I	F	R	Y	C	A	G	S	C	P	Q	E	A	R	T	Q	H	PSP(mouse)

	50										60										70										80										
40	O	K	I	L	K	N	L	S	R	N	R	R	L	V	S	D	K	V	-	G	Q	A	C	C	R	P	I	A	F	D	D	D	L	S	F	L	D	D	N	L	GDNF(human)
40	O	K	I	L	K	N	L	S	R	S	R	R	L	T	S	D	K	V	-	G	Q	A	C	C	R	P	V	A	F	D	D	D	L	S	F	L	D	D	S	L	GDNF(rat)
40	O	K	I	L	K	N	L	S	R	S	R	R	L	T	S	D	K	V	-	G	Q	A	C	C	R	P	V	A	F	D	D	D	L	S	F	L	D	D	N	L	GDNF(mouse)
40	D	L	G	L	R	R	L	R	Q	R	R	R	L	R	R	E	R	V	R	A	Q	P	C	C	R	P	T	A	Y	E	D	E	V	S	F	L	D	A	H	S	NTN(human)
40	D	L	G	L	R	R	L	R	Q	R	R	R	V	R	R	E	R	A	R	A	H	P	C	C	R	P	T	A	Y	E	D	E	V	S	F	L	D	V	H	S	NTN(mouse)
41	S	L	V	L	A	R	L	R	-	-	-	-	-	G	Q	G	R	A	H	G	R	P	C	C	Q	P	T	S	Y	A	D	-	V	T	F	L	D	D	H	S	PSP(rat)
41	S	L	V	L	A	R	L	R	-	-	-	-	-	G	R	G	R	A	H	G	R	P	C	C	Q	P	T	S	Y	A	D	-	V	T	F	L	D	D	Q	H	PSP(mouse)

	90																
79	V	Y	H	I	L	R	K	H	S	A	K	R	C	G	C	.	GDNF(human)
79	V	Y	H	I	L	R	K	H	S	A	K	R	C	G	C	.	GDNF(rat)
79	V	Y	H	I	L	R	K	H	S	A	K	R	C	G	C	.	GDNF(mouse)
80	R	Y	H	T	V	H	E	L	S	A	R	E	C	A	C	.	NTN(human)
80	R	Y	H	T	L	Q	E	L	S	A	R	E	C	A	C	.	NTN(mouse)
75	H	W	Q	Q	L	P	Q	L	S	A	A	A	C	G	C	.	PSP(rat)
75	H	W	Q	Q	L	P											

Figure 15 A

	10	20	30	
1	A L A G S C R L W S L T L P V A E E L G L G Y A S E E K V I F			mPSP
1	A L P G L C R L W S L T L P V A E E L G L G Y A S E E K I I F			rPSP
1	A L S G P C Q L W S L T L S V A E E L G L G Y A S E E K V I F			hPSP
31	R Y C A G S C C P Q E A R T Q H S L V L A R L R G R G R A H G	50		mPSP
31	R Y C A G S C C P Q E V R T Q H S L V L A R L R G R G R A H G			rPSP
31	R Y C A G S C C P R G A R T Q H G L A L A R L Q G Q G R A H G			hPSP
61	R P C C Q P T S Y A D V T F L D D Q H H W Q Q L P Q L S A A	80	90	mPSP
61	R P C C Q P T S Y A D V T F L D D Q H H W Q Q L P Q L S A A			rPSP
61	G P C C R P T R Y T D V A F L D D R H R W Q Q R L P Q L S A A			hPSP
91	A C G C G G			rPSP
91	A C G C G G			rPSP
91	A C G C G G			hPSP

Figure 15B

GROWTH FACTOR	SEQUENCE
0	CCVRQLYIDFRKOLGWK-WIHEPKGYHANFCLGPCPYIWSLDT-----QYSKVLALVNOHNPASAA-PCCV--PQALEPLPIVYVGRKPKV--EQLSNMIVRSCKCS
1	CCLRPLYIDFRKOLGWK-WIHEPKGYANFAGACPYLWSSDT-----OHSRVLSYNTINPEASAS-PCCV--SQDLEPLTILYIGKTPKI--EQLSNMIVKSCCKCS
2	CCVRPLYIDFRQDLGWK-WVHEPKGYANFCSGCPYLRASDT-----THSTVLGLYNTLNPEASAS-PCCV--PQDLEPLTILYVGRTPKV--EQLSNMIVKSCCKCS
3	CCCKOFFVFSFK-DIGWNDWIAPSGYHANYCEGECPSHAG-TSGSSLSFHSVINHYRMRGSHFANLKSCCV--PTKLRPMISMLYDDGQNI--KKDIQNMIVEECGCS
4	CCROOFFIDFR-LIGWNDWIAPTYGNYCEGSCPAYLAG-VPGSASSFHTAVNQYRMRGLNP-GTVNSCCI--PTKLSMTSMLYFDDEYNIV-KRDVPMNIVEECGCA
5	CRRVKEQVDFN-LIGWGSWIIYPKQYNAIRCEGECNPVGEFFHT----NHAYIQSLKRYQPHR-VPSTCCA--PVKTKPLSMLYVDNGR--VLLEHKKDMIVEECGCL
6	CKRHPLYVDFS-DVGWNDWIAPPGYHAFYCHGECFFPLADHLNST----NHAIVQTLVNSVNS-K-IPKACCV--PTELSAISMLYLDENEKVWLK-NYQDMVVEGGCR
7	CRRHSLYVDFS-DVGWNDWIAPPGYQAFYCHGDCPFPLADHLNST----NHAIVQTLVNSVNS-S-IPKACCV--PTELSAISMLYLDYDKVWLK-NYQEMVVEGGCR
8	CRRHSLYVDFS-DVGWDDWIAPGLDAYYCHGKCPFLADHFNST----NHAVQTLVNNMNPBK-VPKACCV--PTQLDSVAMLYLNDOSTVWLK-NYQEMTVVGGCR
9	CKKHLYVDFS-DVGWQDWIIAPEGYAAFYCDGECFPLNAHMMNAT----NHAIVQTLVHLMNPEY-VPKPCCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRSCGCH
10	CRKHLYVDFS-DVGWQDWIIAPKGYAANYCDGECFPLNAHMMNAT----NHAIVQTLVHLMNPEY-VPKPCCA--PTKLNAISVLYFDDSSNVILK-KYRNMVVRACGCH
1	CKKHLYVDFS-DVGWQDWIIAPEGYAAAYCEGECFPLNSYMMNAT----NHAIVQTLVHFMNPEY-VPKPCCA--PTQLNAISVLYFDDSSNVILK-KYRNMVVRACGCH
2	CRRHLYVDFS-DVGWLDWIAPQGYSAAYCEGECFPLDSCMNAT----NHAIQSLVHLMKPNV-VPKACCA--PTKLSATSVLYDSSNNVILK-KHRNMVVKACGCH
3	COMQTLYIDFK-DLGWHDWIAPQGYGAFYCSGECNFPPLNAHMMNAT----NHAIVQTLVHLEPKK-VPKPCCA--PTRLGALPVLHLNDENVNK-KYRNMIVKSGGCH
4	CARRYLVDFKA-DIGWSEWIIISPKSFDAYYCSGACQFPMPSLKPS-----NHATIQSIVRAVGVPVGIPEPCCV--PEKMSLSILFFDENKNVWLK-VPMNMTVESACR
5	CKKRHLVVEFK-DVGWQNWIIAPQGYMANYCYGECPYLTELNGS-----NHAIQTLVHSIEPED-IPLPCCV--PTKMSPIISMLFYDNDNDNVLR-HYENMAVDEGCR
6	CRARLVYSFR-EVGWHRWIIAPRGFLANYCGQCALPVALSGSGGPPALNHAVALRMHAAAPGA-ADLPCCV--PARLSPISVLFEDNSDNVLR-QYEDMVVDEGCR
7	CHRHOLFINFO-DLGWHLKWIAPKGFMANVCHGECFPMTTYLNSS-----NYAFMQALMHMADP-K-VPKAVCV--PTKLSPIISMLYQDSKNVILR-HYEDMVVDEGCG
8	CRRTSLVHNFK-ETGWDSWIIAPKDYAEFECKGGCFPLTDNVTP-----KHAIVQTLVHLQNPBK-ASKACCV--PTKLDASISILYKDDAGVPTLIYNYEGMKVAECGR
9	CHRVALLNISF-QELGWERWIIYPPSFIFHYCHGGGLHIPNLSLPVPGAPPTPAQYSSL-----PGAOPCCAALPGTMRPLHVRTTSDGGYSFKYETVPNLLTQHCACI
10	CALRELSVDLRAERS-----VLIPETYQANNCCGACGWQSDR-----NPRYGNHVVLLKMQARGATLARPPCCV--PTAYT--GKLLISLSEERISAHVPMNMTATEGGR
1	CELHDFSLSFS-QLKWDNWIAPHSYNPSYCKGDCPSAVSHRYGSPV-----HTMVQNMITYE-KLDPSVPSPSCV--PGKYSPLSVLTIEPDGSIAYK-EYEDMMATSCTR
2	CVLTAIHLNVT-DLGLG--YETKEELIFRYCSGSD-AAETTYDKILKNLSRN-----RRLVSDKV-GQACCRPIAFD-DDLSFL-----DDNLVYHILRKHSKRCCGI
3	CGLRELEVRVS-ELGLG--YASDETVLFRYCAGACE-AAARVYDLGLRRLRQR-----RRLRRERVRAQPCCRPTAYE-DEVSFL-----DAHSRYHTVHLSARECACV

FIGURE 16

1	ATGGCTGCAG TACCGACGTC	GAAGACTTCG CTTCTGAAGC	GATCCTGTGT CTAGGACACA	CTGCTGCTCC GACGACGAGG	TGTCCTTGCA ACAGGAACGT	CCCGAGCCTC GGGCTCGGAG
61	GGCTGGGTCC CCGACCCAGG	TTGATCTTCA AACTAGAAGT	AGAGGCTTCT TCTCCGAAGA	GTGGCAGATA CACCGTCTAT	AGCTCTCATT TCGAGAGTAA	TGGGAAGATG ACCCTTCTAC
121	GCAGAGACTA CGTCTCTGAT	GAGGGACCTG CTCCCTGGAC	GACGCCCCAT CTGCGGGGTA	CAGGGTAAGA GTCCCATTCT	ATTECTGGGG TAAGGACCCC	GCCTCCCGAC CGGAGGGCTG
181	TCCCCAATTC AGGGGTAAAG	CTTCTCTCAA GAAGAGAGTT	AGCCCTCACT TCGGGAGTGA	TTGCCTTACA AACGGAATGT	ATCCTACTCT TAGGATGAGA	ACCTTGCACT TGGAACGTGA
241	AGGTAACAAC TCCATTGTTG	CATGTCCGTC GTACAGGCAG	TTCCAAGAGC AAGGTTCTCG	CTTGGCTGGT GAACCGACCA	TCATGCCGAC AGTACGGCTG	TGTGGAGCCT ACACCTCGGA
301	GACCCTACCA CTGGGATGGT	GTGGCTGAGC CACCGACTCG	TGGGCCTGGG ACCCGGACCC	CTATGCCTCG GATACGGAGC	GAGGAGAAGG CTCCTCTTCC	TCATCTTCCG AGTAGAAGGC
361	ATACTGTGCT TATGACACGA	GGCAGCTGTC CCGTCGACAG	CCCAAGAGGC GGGTTCTCCG	CCGTACCCAG GGCATGGGTC	CACAGTCTGG GTGTCAGACC	TACTGGCCCC ATGACCGGGC
421	GCTTCGAGGG CGAAGCTCCC	CGGGGTGAG GCCCCAGCTC	CCCATGGCCG GGGTACCGGC	ACCCTGCTGC TGGGACGACG	CAGCCCACCA GTCGGGTGGT	GCTATGCTGA CGATACGACT
481	TGTGACCTTC ACACTGGAAG	CTTGATGATC GAACTACTAG	AGCACCATTG TCGTGGTAAC	GCAGCAGCTG CGTCGTCGAC	CCTCAGCTCT GGAGTCGAGA	CAGCTGCAGC GTCGACGTCG
541	TTGTGGCTGT AACACCGACA	GGTGGCTGAA CCACCGACTT	GGAGGCCAGT CCTCCGGTCA	CTGGTGTCTC GACCACAGAG	AGAATCACAA TCTTAGTGTT	GCATGAGACA CGTACTCTGT
601	GGCTGGGCTT CCGACCCGAA	TGAAAGGCTC ACTTTCCGAG	AGGTGACATT TCCACTGTAA	ACTAGAAATT TGATCTTTAA	TGCATAGGTA ACGTATCCAT	AAGATAAGAA TTCTATTCTT
661	GGGAAAGGAC CCCTTTCCTG	CAGGGGTTTT GTCCCCAAAA	TTGTTTCTTT AACAAAGAAA	CTTTGCTTGC GAAACGAACG	TTGTTAGTTT AACAAATCAA	TTTTTTTTTT AAAAAAAAAA
721	TTT AAA					

Figure 17A

1	ATGGCTGCAG	GAAGACTTCG	GATCCTGTGT	CTGCTGCTCC	TGTCCTTGCA	CCCGAGCCTC
	TACCGACGTC	CTTCTGAAGC	CTAGGACACA	GACGACGAGG	ACAGGAACGT	GGGCTCGGAG
1	M A A G	R L R	I L C	L L L L	S L H	P S L
61	GGCTGGGTCC	TTGATCTTCA	AGAGGCTTCT	GTGGCAGATA	AGCTCTCATT	TGGGAAGATG
	CCGACCCAGG	AACTAGAAGT	TCTCCGAAGA	CACCGTCTAT	TCGAGAGTAA	ACCCTTCTAC
21	G W V / L	D L Q	E A S	V A D K	L S F	G K M
				↓		
121	GCAGAGACTA	GAGGGACCTG	GACGCCCCAT	CAGGGTAACA	ACCATGTCCG	TCTTCCAAGA
	CGTCTCTGAT	CTCCCTGGAC	CTGCGGGGTA	GTCCCATTGT	TGGTACAGGC	AGAAGGTTCT
41	A E T R	G T W	T P H	Q G N N	H V R	L P R
181	GCCTTGGCTG	GTTTCATGCCG	ACTGTGGAGC	CTGACCCTAC	CAGTGGCTGA	GCTGGGCCTG
	CGGAACCGAC	CAAGTACGGC	TGACACCTCG	GACTGGGATG	GTCACCGACT	CGACCCGGAC
61	A L A G	S C R	L W S	L T L P	V A E	L G L
241	GGCTATGCCT	CGGAGGAGAA	GGTCATCTTC	CGATACTGTG	CTGGCAGCTG	TCCCCAAGAG
	CCGATACGGA	GCCTCCTCTT	CCAGTAGAAG	GCTATGACAC	GACCGTCGAC	AGGGGTTCTC
81	G Y A S	E E K	V I F	R Y C A	G S C	P Q E
301	GCCCGTACCC	AGCACAGTCT	GGTACTGGCC	CGGCTTCGAG	GGCGGGGTCG	AGCCCATGGC
	CGGGCATGGG	TCGTGTCAGA	CCATGACCGG	GCCGAAGCTC	CCGCCCCAGC	TCGGGTACCG
101	A R T Q	H S L	V L A	R L R G	R G R	A H G
361	CGACCCTGCT	GCCAGCCAC	CAGCTATGCT	GATGTGACCT	TCCTTGATGA	TCAGCACCAT
	GCTGGGACGA	CGGTCGGGTG	GTCGATACGA	CTACACTGGA	AGGAACTACT	AGTCGTGGTA
121	R P C C	Q P T	S Y A	D V T F	L D D	Q H H
421	TGGCAGCAGC	TGCCTCAGCT	CTCAGCTGCA	GCTTGTGGCT	GTGGTGGCTG	A
	ACCGTCGTCG	ACGGAGTCGA	GAGTCGACGT	CGAACACCGA	CACCACCGAC	T
141	W Q Q L	P Q L	S A A	A C G C	G G	.

Figure 17B

8642221122498

1 ATGGCTGCAG GAAGACTTCG GATCTTGTTT CTGCTGCTCC TGTCTTTGCA CCTGGGCCTT
 TACCGACGTC CTTCTGAAGC CTAGAACAAA GACGACGAGG ACAGGAACGT GGACCCGGAA
 61 GGCTGGGTCC TTGATCTTCA AGAGGCTCCT GCGGCAGATG AGCTCTCATC TGGGAAAATG
 CCGACCCAGG AACTAGAAGT TCTCCGAGGA CGCCGTCTAC TCGAGAGTAG ACCCTTTTAC
 121 GCAGAGACTG GAAGGACCTG GAAGCCCCAT CAGGGTAAGA ATTCTTGGGG GCCTCCTAAC
 CGTCTCTGAC CTTCTGGAC CTTCTGGGTA GTCCCATTTCT TAAGAACCCC CGGAGGATTG
 181 TCTACAGTTC TTCCTCTCAA AGCCCTCACT TTGCCTCACA ATCCTATTCT ACCTTGCACT
 AGATGTCAAG AAGGAGAGTT TCGGGAGTGA AACGGAGTGT TAGGATAAGA TGGAACGTGA
 241 AGGTAACAAC AATGTCCGCC TTCCAAGAGC CTTACCTGGT TTGTGCCGGC TGTGGAGCCT
 TCCATTGTTG TTACAGGCGG AAGGTTCTCG GAATGGACCA AACACGGCCG ACACCTCGGA
 301 GACCCTACCA GTGGCTGAGC TTGGCCTGGG CTATGCCTCA GAGGAGAAGA TTATCTTCCG
 CTGGGATGGT CACCGACTCG AACCGGACCC GATACGGAGT CTCCTCTTCT AATAGAAGGC
 361 ATACTGTGCT GGCAGCTGTC CCCAAGAGGT CCGTACCCAG CACAGTCTGG TGCTGGCCCCG
 TATGACACGA CCGTCGACAG GGGTTCTCCA GGCATGGGTC GTGTCAGACC ACGACCGGGC
 421 TCTTCGAGGG CAGGGTCGAG CTCATGGCAG ACCTTGCTGC CAGCCCACCA GCTATGCTGA
 AGAAGCTCCC GTCCCAGCTC GAGTACCGTC TGAACGACG GTCGGGTGGT CGATACGACT
 481 TGTGACCTTC CTTGATGACC ACCACCATTG GCAGCAGCTG CCTCAGCTCT CAGCCGCAGC
 AACTGGAAG GAACTACTGG TGGTGGTAAC CGTCGTCGAC GGAGTCGAGA GTCGGCGTCG
 541 TTGTGGCTGT GGTGGCTGA
 AACACCGACA CCACCGACT

Figure 18A

09620617-12499

1	ATGGCTGCAG	GAAGACTTCG	GATCTTGTTT	CTGCTGCTCC	TGTCCTTGCA	CCTGGGCCTT
	TACCGACGTC	CTTCTGAAGC	CTAGAACAAA	GACGACGAGG	ACAGGAACGT	GGACCCGGAA
1	M A A G	R L R	I L F	L L L L	S L H	L G L
61	GGCTGGGTCC	TTGATCTTCA	AGAGGCTCCT	GCGGCAGATG	AGCTCTCATC	TGGGAAAATG
	CCGACCCAGG	AACTAGAAGT	TCTCCGAGGA	CGCCGTCTAC	TCGAGAGTAG	ACCCTTTTAC
21	G W V L	D L Q	E A P	A A D E	L S S	G K M
121	GCAGAGACTG	GAAGGACCTG	GAAGCCCCAT	CAGGGTAACA	ACAATGTCCG	CCTTCCAAGA
	CGTCTCTGAC	CTTCCTGGAC	CTTCGGGGTA	GTCCCATTTGT	TGTTACAGGC	GGAAGGTTCT
41	A E T G	R T W	K P H	Q G N N	N V R	L P R
181	GCCTTACCTG	GTTTGTGCCG	GCTGTGGAGC	CTGACCCTAC	CAGTGGCTGA	GCTTGGCCTG
	CGGAATGGAC	CAAACACGGC	CGACACCTCG	GACTGGGATG	GTCACCGACT	CGAACCGGAC
61	A L P G	L C R	L W S	L T L P	V A E	L G L
241	GGCTATGCCT	CAGAGGAGAA	GATTATCTTC	CGATACTGTG	CTGGCAGCTG	TCCCCAAGAG
	CCGATACGGA	GTCTCCTCTT	CTAATAGAAG	GCTATGACAC	GACCGTCGAC	AGGGGTTCTC
81	G Y A S	E E K	I I F	R Y C A	G S C	P Q E
301	GTCCGTACCC	AGCACAGTCT	GGTGCTGGCC	CGTCTTCGAG	GGCAGGGTCG	AGCTCATGGC
	CAGGCATGGG	TCGTGTCAGA	CCACGACCGG	GCAGAAGCTC	CCGTCCCAGC	TCGAGTACCG
101	V R T Q	H S L	V L A	R L R G	Q G R	A H G
161	AGACCTTGCT	GCCAGCCCAC	CAGCTATGCT	GATGTGACCT	TCCTTGATGA	CCACCACCAT
	TCTGGAACGA	CGGTCGGGTG	GTCGATACGA	CTACACTGGA	AGGAACTACT	GGTGGTGGTA
121	R P C C	Q P T	S Y A	D V T F	L D D	H H H
141	TGGCAGCAGC	TGCCTCAGCT	CTCAGCCGCA	GCTTGTGGCT	GTGGTGGCTG	A
	ACCGTCGTCG	ACGGAGTCGA	GAGTCGGCGT	CGAACACCGA	CACCACCGAC	T
141	W Q Q L	P Q L	S A A	A C G C	G G	.

Figure 18B

PCB6
Rat PSP
Murine PSP
Mature PSP (E.coli)
COS cell lysate

46 kd —
30 kd —
21 kd —
14 kd —
6 kd —



Figure 19

09220517 122498

Sub

6

FIGURE 20A

PSP/NTN (SEQ ID NO:¹⁴¹137)

ALAGSCLWSLTLPVAELGLGYASEEKVIFRYCAGSCPQEARTQHSLVLA 50
↓
RLRGRGRAHGRPCCRPTAYEDEVSFLDVHSRYHTLQELSARECACV 96

FIGURE 20B

NTN/PSP (SEQ ID NO:¹⁴²142)

PGARPCGLRELEVRVSELGLGYTSDETVLFRYCAGACEAAIRIYDLGLRR 50
↓
LRQRRRVRRERARAHPCCOPTSYADVTFLLDDQHHWQQLPQLSAAACGCGG 100

864227" / F902260

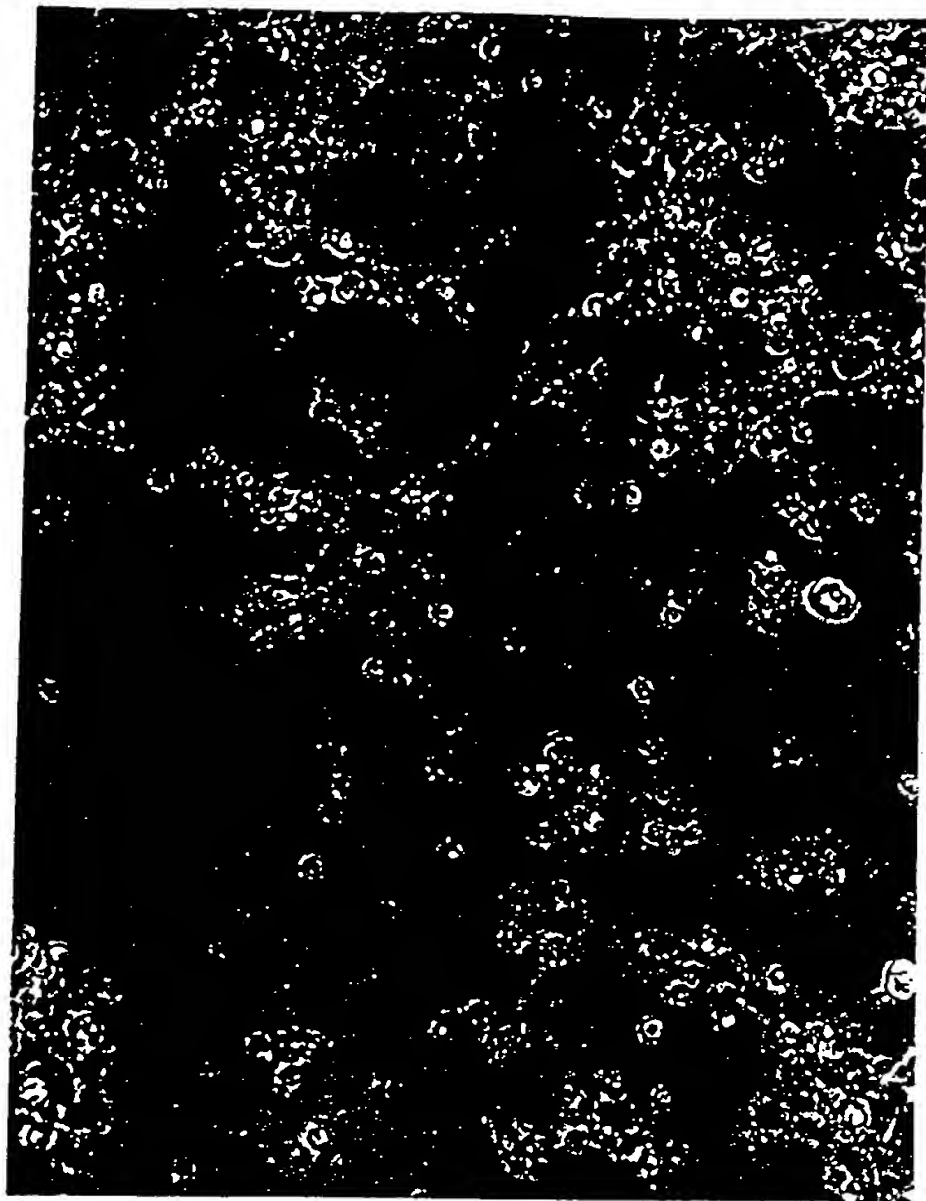


Figure 21a

86422T" 2F902260



Figure 21b

09220617-12498
864227-47902260

TOH labeled cells in E14 mesencephalic cultures

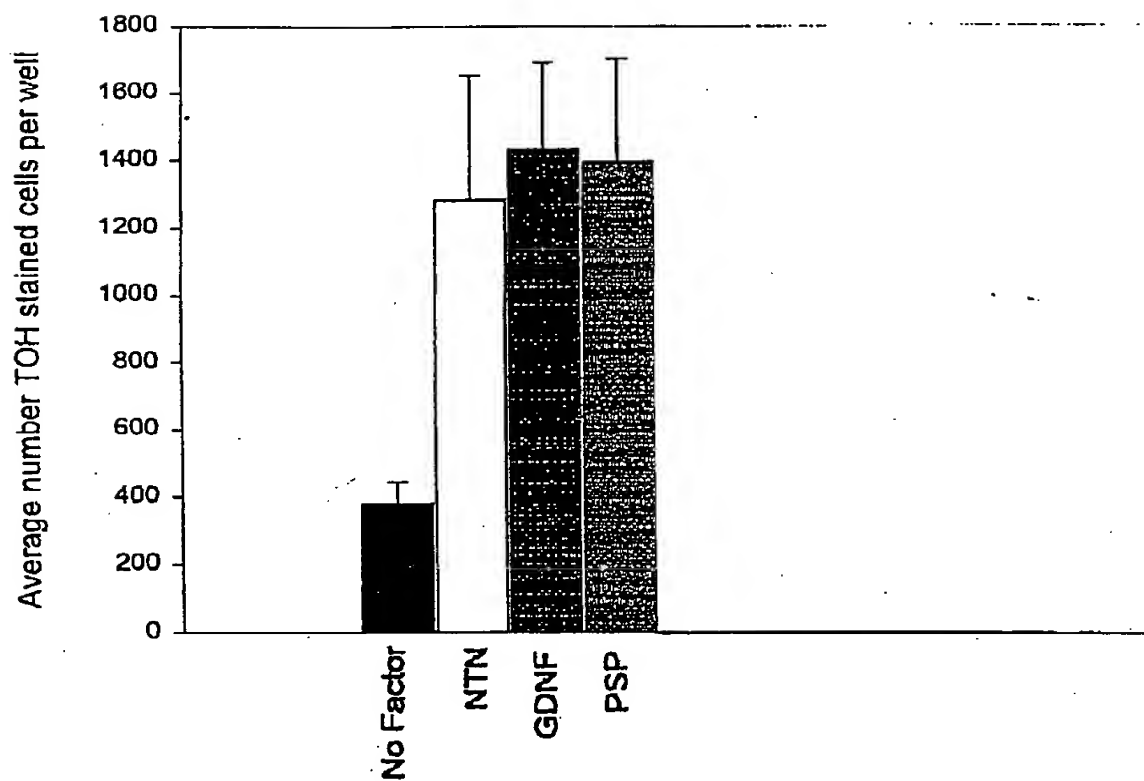


Figure 22

09220617 122498

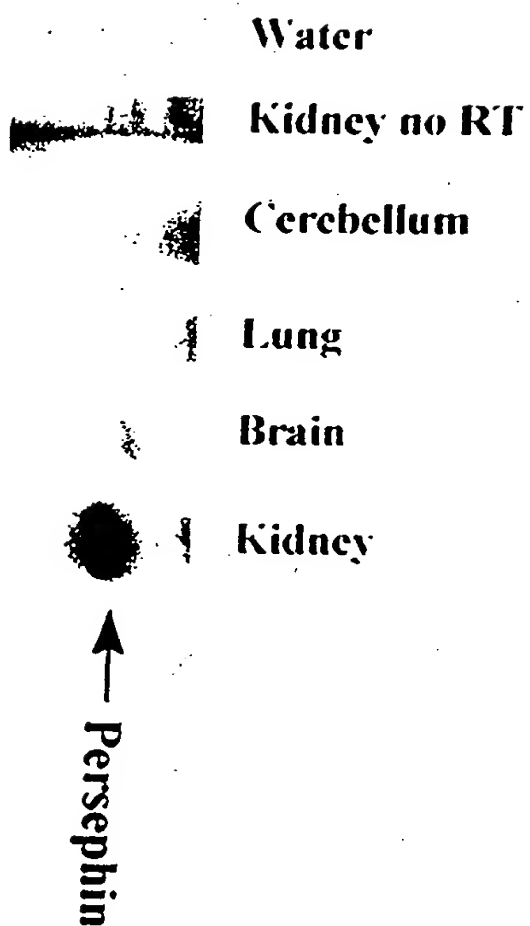


Figure 23

